Tracking malaria transmission at the antenatal clinic

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The development of resistance to sulfadoxine-pyrimethamine is a threat to the effectiveness of intermittent preventive treatment for malaria during pregnancy (IPTp), especially in areas of east Africa where the A581G molecular marker denoting super-resistance is prevalent.[1,2] As a result, alternative strategies for protection from malaria during pregnancy are being explored.[3] One idea, intermittent screening and treatment during pregnancy (ISTp), involves a rapid diagnostic test (RDT) for the screening of women who present to antenatal clinics and use of highly effective artemisinin-based drugs to treat those with malaria parisitaemia.

As Anna Maria van Eijk and colleagues[4] highlight in *The Lancet Global Health*, the inclusion of rapid diagnostic tests for malaria in to routine care at antenatal clinics could provide a valuable and extremely convenient source of information about local patterns in malaria transmission. Further, such a strategy has become feasible since the price of RDT has decreased sharply. However, for these data to be useful as a surveillance tool we must understand the relation between prevalence in pregnant women and the endemicity of infection in the general population, especially in children who are the most commonly sampled sentinels of infection and who bear most of the malaria burden.

This relationship will be complicated: the prevalence of malaria infection in non-pregnant adults is lower than that for children within the same setting,[5] a finding probably related to the differing levels of immunity in the adult and child populations. Since immunity depends on previous exposure and also the longevity of infection,[6,7] it will, then, vary with transmission intensity.[5]

Pregnancy provides a second layer of complexity: around the time that maternal blood flows into the placenta, the *Plasmodium falciparum* parasite (the most prevalent and pathogenic species of plasmodia) is able to sequester within the intervillous space.[8] In women who have not been exposed to malaria during a previous pregnancy, the parasite can replicate to very high densities. Although women in their second or subsequent pregnancies will probably be exposed to a similar risk of infection as that in their first pregnancy,[9] acquired immunity to placental parasites will allow multigravidae to more effectively control parasite replication within the placenta than was possible in their first pregnancy.[8] Because parasite biomass is likely to be heavily linked to the level of antigen the diagnostic is designed to detect (usually histidine-rich protein 2 (HRP-2),[10] it seems reasonable to expect that malaria prevalence in later pregnancies will also follow a distinct pattern dependent on transmission intensity.

The strong correlation between infection in pregnant women and children established by van Eijk and colleagues,[4] using extensive large-scale cross-sectional prevalence data in the two groups, is grounds for optimism about the usefulness of these data as an indicator of transmission. Moreover, results of van Eijk and colleagues' analysis provides insight into the next steps to follow in the search of a metric that can be readily used. Their results suggest that, in areas of low transmission, prevalence in pregnant women is likely to be very similar to that in young children, but that, as transmission reaches higher intensities, cross-sectional prevalence surveys of pregnant women will increasingly underestimate those in children.

Although based on fewer data, malaria prevalence in primigravidae seems to be a much more reliable indicator in highly endemic settings, consistently representing approximately 86% of that in children, including settings where up to 80% of children have parasitaemia detectable by microscopy. This finding suggests another important potential intersection between achieving adequate care for malaria during pregnancy and monitoring transmission: primigravidae provide the most accurate information about the nature of transmission and are also most likely to have negative health outcomes as a result of infection, so, therefore, are most likely to benefit from a strategy that leads to improved care when infection during pregnancy is detected.

Understanding how advances in malaria diagnostics can be best used to benefit pregnant women is, however, not straightforward. RDTs are not perfectly sensitive in the detection of infection during pregnancy.[9] Further, antimalarial drugs, including sulfadoxine-pyrimethamine, provide a period of prophylaxis against infection—meaning that, under the IPTp protocol, even women who do not have malaria parisitaemia detected

at an antenatal clinic would receive presumptive treatment and benefit from decreased levels of exposure to malaria as a result.

Understanding how (or whether) the diagnosis of malaria infection in pregnancy can be of direct benefit to pregnant women, either in terms of safety, efficacy, effectiveness, or acceptability, of an intervention will be crucial in determining whether pregnant women at antenatal clinics are a viable resource for malaria surveillance.

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